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| 10/507,129 | 04/11/2005 | Satoshi Saito | 03419.0023-00 | 8898 |
| 22852 7590 03/19/2008 FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP 901 NEW YORK AVENUE, NW WASHINGTON, DC 20001-4413 | | | | |
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| | | | LONG, SCOTT | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/507,129

Applicant(s)

SAITO ET AL.

Examiner

SCOTT D. LONG

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 16-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 16-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 November 2007 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB08)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date 11/20/2007.

DETAILED ACTION

The examiner acknowledges receipt of Applicant's Remarks, Claim & Specification amendments, filed on 20 November 2007.

Claim Status

Claims 1-7 and 16-18 are pending. Claims 1, 3-7, and 16-18 are amended.
Claim 8-15 and 19 are cancelled. Claims 1-7 and 16-18 are under current examination.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 20 November 2007 consisting of 1 sheet(s) is/are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

Priority

This application claims benefit as a 371 of PCT/JP03/02833 0 (filed 3/11/2003). This application also claims benefit from the foreign application JAPAN 2002-065880 (filed 03/11/2002). The applicant has provided an English translation of the foreign application JAPAN 2002-065880. Therefore, the instant application has been granted the benefit date, 3/11/2002, from the foreign application JAPAN 2002-065880.

Specification

This applicant has submitted amendments to the specification in which the phrase "sequence number" has been replaced by "SEQ ID NO:" thereby overcoming the basis of the examiner's objection to the specification. Therefore, the examiner hereby withdraws the objection to drawings.

Drawings

The replacement drawing for Figure 9 satisfactorily overcomes the outstanding objection to drawings. Therefore, the examiner hereby withdraws the objection to drawings.

Response to Arguments - Claim Objections

Applicant's arguments, see page 14 and Claim amendments, filed 20 November 2007, with respect to claims 6, 7, and 17 have been fully considered and are persuasive. The applicant has amended the claims so that "Saccharomyces" is correctly spelled. Therefore, the examiner hereby withdraws the objection to claims 6-7 and 17.

In addition, the objection to claims 3-5 is withdrawn because the phrase "sequence number" has been replaced by "SEQ ID NO:" thereby overcoming the basis of the examiner's objection to these claims.

Response to Arguments - Claim Rejections 35 USC 112

Response to Arguments – (35 USC 112, 2nd paragraph)

Applicant's arguments, see pages 14-15 and Claim amendments, filed 20 November 2007, with respect to claims 1-7 and 16-18 have been fully considered and are persuasive. The claim amendments have overcome all indefiniteness. Therefore, the examiner hereby withdraws the rejection of claims 1-7 and 16-18 under 35 USC 112, 2nd paragraph.

Response to Arguments – Written Description (35 USC 112, 1st paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 remain rejected under 35 USC 112, 1st paragraph for the reasons of record and the comments below.

Applicant's arguments see pages 15-17 and Claim amendments, filed 20 November 2007, with respect to claims 1-7 and 16-18 have been fully considered but they are only partially persuasive.

The applicant argues that the knowledge in the art provides support for the recited genus of lactate dehydrogenase homologues and pyruvate decarboxylase promoters in claims 1-7 and 16-18. In support of this position, the applicant has provided evidentiary references Li et al. (Journal of Biological Chemistry. 1983, 258(11):

7017-7028) and Kellermann et al. (Nucleic Acids Research, 1986, 14(22): 8963-8977), showing that the structure and function for lactate dehydrogenase genes and pyruvate decarboxylase promoters was known in the art at the time the instant application was filed. The examiner accepts this argument as sufficient to overcome the portion of the written description rejection based on lack of possession of the genus of lactate dehydrogenase homologues and the genus of pyruvate decarboxylase promoters. Therefore, the examiner hereby withdraws this portion of the written description rejection.

However, the examiner does not find persuasive the applicant's argument regarding possession of a genus of transformants encompassing insects, animals, and plants. While it is well established that transgenic animals and plants have been made for years, the instant application contains no examples of these organisms which contains the genetic modifications recited in the instant claims. Therefore, the examiner concludes the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed genus of "transformants" commensurate to its scope at the time the application was filed. Claims 16-18 have been amended to limit the scope of the transformants of the *Saccharomyces* family. Therefore, the examiner believes the specification to have sufficient evidence of possession for this scope. Accordingly, the examiner withdraws the lack of possession rejection for claims 16-18.

Therefore, the rejection of claims 1-7 under 35 USC 112, first paragraph (written description) is hereby maintained.

Response to Arguments – Lack of Enablement (35 USC 112, 1st paragraph)

Applicant's arguments see pages 17-20, filed 20 November 2007, with respect to claims 16-18 have been fully considered and they are persuasive.

The applicant indicates a citation of the specification which indicates that the isolated nucleic acids identified as hybridizing to the *S. cerevisiae* pyruvate decarboxylase 1 promoter require "promoter activity" like that of SEQ ID NO:2 (Remarks, page 19 and Spec. page 6, lines 40-46). The examiner finds this sufficiently persuasive to overcome the lack of enablement rejection based on isolated nucleic acids identified by hybridizing to the *S. cerevisiae* pyruvate decarboxylase 1 promoter.

Therefore, the rejection of claims 16-18 under 35 USC 112, first paragraph (lack of enablement) is hereby withdrawn.

Response to Arguments - Claim Rejections 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-4, 6-7 and 16-18 remain rejected as anticipated by Porro et al (US-6429006) under 35 USC 102(e) and by Porro et al. (WO99/14335) under 35 USC 102(b), for the reasons of record.

Applicant's arguments (see pages 21-22) and Claim amendments, filed 20 November 2007, with respect to claims 1-4, 6-7 and 16-18 have been fully considered but are unpersuasive.

The applicant traverses the instant rejection on the following grounds:

The applicant argues that Porro et al. do not teach "each and every element as set forth in the claims 1 and 16. The applicant does not specifically indicate which teachings are not present in Porro et al. Therefore, the examiner will include all the specific teachings of Porro et al. recited in the First Office Action (filed 6/20/2007) at the end of this section.

However, the applicant does contrast the teachings of Porro et al. with the instant invention (Remarks, page 22). The applicant states, "the instantly claimed invention required that the DNA encoding lactate dehydrogenase is incorporated into the downstream (3') side of the pyruvate decarboxylase gene promoter on the host

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chromosome.” (Remarks, page 22, lines 3-5). Although the instant claim language does not exactly recite this specific language, the examiner believes that Porro et al. teaches these limitations. Porro et al. teach, “yeast strains...transformed with at least one copy of a gene coding for lactic dehydrogenase (LDH) functionally linked to promoter sequences allowing the expression of said gene in yeasts” (col.2, lines 30-35). Porro et al. teach, “yeast strains having...a reduced pyruvate decarboxylase activity and transformed with...a gene coding for lactic dehydrogenase (LDH) functionally linked to promoter sequences” (col.2, lines 36-40). Porro et al. teach any yeast promoter...may be used according to the invention...the promoter of pyruvate decarboxylase gene of *K. lactis* (KIPDC) is particularly preferred (col.7, lines 1-10). Porro et al. further teach, “Pyruvate decarboxylase gene promoters...are particularly preferred” (col.7, lines 15-17). Therefore, Porro et al. teach that lactate dehydrogenase gene can be expressed using a pyruvate decarboxylase promoter.

The applicant further contrasts the teachings of Porro with the instant invention, suggesting that the instant invention “produces large volumes of lactic acid while simultaneously destroying the pyruvate decarboxylase gene that suppresses the production of lactic acid.” (Remarks, page 22, lines 6-8). The applicant notes that these limitations are not explicit in claim 1. In addition to the teachings of Porro et al. recited above, Porro et al. also describe making a triple deletion of the pyruvate decarboxylase genes encoding PDC1, PDC5, and PDC6, using homologous recombination (col.16, lines 54-67 and col.17, lines 1-20). Porro et al. also teach chromosomally integrated vectors and homologous recombination of genes (col.6, lines 1-4 and col.10, line 38).

Furthermore, the applicant suggests "Unlike Porro, lactic acid be can efficiently produced by the instantly claimed invention with only a single copy of the LDG gene and without suppression of pyruvate decarboxylase." (Remarks, page 22, lines 16-18). This statement seems to contradict the applicant's earlier assertion, "Applicants discovered that the instant invention advantageously produces large volumes of lactic acid while simultaneously destroying the pyruvate decarboxylase gene that suppresses the production of lactic acid" (Remarks, page 22, lines 6-9). The examiner notes that the instant claim 16 is broadly written to recite "the structural gene of the pyruvate decarboxylase 1 on the host chromosome has been destroyed" (claim 16). Porro et al. teach "higher yields (>80% g/g) in the production of lactic acid may be obtained by engineered yeast....To this purpose, the invention also provides transformed yeast cells having an increased LDH activity, for instance as a consequence of an increased LDH copy number per cell or of the use of stronger promoters controlling LDH expression" (col., lines). Porro et al. describe making a triple deletion of the pyruvate decarboxylase genes encoding PDC1, PDC5, and PDC6, using homologous recombination (col.16, lines 54-67 and col.17, lines 1-20). In addition, Porro et al teach "The invention refers to yeast strains transformed with at least one copy of a gene coding for lactic dehydrogenase (LDH) and further modified for the production of lactic acid with high yield and productivity" (col. 1, lines 6-9). Therefore, Porro teach both (1) efficient production of large volumes of lactic acid by yeast expressing lactate dehydrogenase using a high expressing promoter and (2) destruction of pyruvate decarboxylase gene. The examiner believes this is what the instant claims recite.

Therefore, the examiner finds the applicant's arguments unpersuasive and the rejection of claims 1-4, 6-7 and 16-18 remain rejected as anticipated by Porro et al (US-6429006) under 35 USC 102(e) and by Porro et al. (WO99/14335) under 35 USC 102(b), for the reasons of record and the comments above.

In addition, the examiner reiterates his previous rejection:

Claims 1-4, 6-7 and 16-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Porro et al (US-6,429,006; issued 6 August 2002).

Claim 1 is directed to a transformant into which has been incorporated a DNA for coding a foreign protein having lactate dehydrogenase activity and provided with pyruvic acid substrate affinity that equals or exceeds the pyruvic acid substrate affinity of the pyruvate decarboxylase inherent in the host organism, wherein the DNA for coding the aforementioned foreign protein has been controllably incorporated by the promoter of the pyruvate decarboxylase gene on the host chromosome or by a homologue of said promoter that replaces said promoter. Porro et al. teach, "yeast strains...transformed with at least one copy of a gene coding for lactic dehydrogenase (LDH) functionally linked to promoter sequences allowing the expression of said gene in yeasts" (col.2, lines 30-35). Porro et al. teach, "yeast strains having...a reduced pyruvate decarboxylase activity and transformed with...a gene coding for lactic dehydrogenase (LDH) functionally linked to promoter sequences" (col.2, lines 36-40). Porro et al. teach any yeast promoter...may be used according to the invention...the promoter of pyruvate decarboxylase gene of *K. lactis* (KIPDC) is particularly preferred (col.7, lines 1-10). Porro et al. further teach, "Pyruvate decarboxylase gene promoters...are particularly

preferred" (col.7, lines 15-17). Porro et al. describe making a triple deletion of the pyruvate decarboxylase genes encoding PDC1, PDC5, and PDC6, using homologous recombination (col.16, lines 54-67 and col.17, lines 1-20). Porro et al. further teach that "PDC genes are highly conserved among different yeast genera" (col.4, lines 44-45), suggesting that the invention of Porro et al. satisfy all the limitations of claim 1.

Claim 2 is directed to the transformant according to claim 1, wherein the aforementioned foreign protein is a bovine-derived lactate dehydrogenase or its homologue. Porro et al. teach, "the gene coding for lactate dehydrogenase may be of any species (e.g. mammalian, such as bovine)" (col.5, lines 27-28).

Claim 3 is directed to the transformant according to claim 1, wherein the aforementioned foreign protein is a protein comprised of the amino acid sequence shown in sequence number 1 or its homologue. SEQ ID NO:1 is the bovine lactate dehydrogenase gene. Clearly, Porro et al. contemplates the amino acid encoded this gene or its homologue. Porro et al. teach, "the gene coding for lactate dehydrogenase may be of any species (e.g. mammalian, such as bovine)" (col.5, lines 27-28).

Claim 4 is directed to the transformant according to claim 3, wherein the aforementioned foreign protein is coded by the DNA sequence shown in sequence number 3. Clearly, Porro et al. contemplates this gene or its homologue. Porro et al. teach, "the gene coding for lactate dehydrogenase may be of any species (e.g. mammalian, such as bovine)" (col.5, lines 27-28).

Claim 6 is directed to the transformant according to any of claims 1 through 5, wherein the aforementioned host organism belongs to the *Saccharomyces* family.

Claim 7 is directed to the transformant according to any of claims 1 through 5, wherein the aforementioned host organism is *Saccharomyces cerevisiae*. Porro et al. teach transformed yeast, *Saccharomyces cerevisiae*.

Claim 16 is directed to a transformant into which the DNA for coding the bovine-derived lactate dehydrogenase or its homologue has been controllably incorporated by the promoter of the pyruvate decarboxylase 1 gene on the host chromosome of the *Saccharomyces* family or by a homologue of said promoter that replaces said promoter, and wherein the structural gene of the pyruvate decarboxylase 1 on the host chromosome has been destroyed. Porro et al. teach, "yeast strains...transformed with at least one copy of a gene coding for lactic dehydrogenase (LDH) functionally linked to promoter sequences allowing the expression of said gene in yeasts" (col.2, lines 30-35). Porro et al. teach, "yeast strains having...a reduced pyruvate decarboxylase activity and transformed with...a gene coding for lactic dehydrogenase (LDH) functionally linked to promoter sequences" (col.2, lines 36-40). Porro et al. teach any yeast promoter...may be used according to the invention...the promoter of pyruvate decarboxylase gene of *K. lactis* (KIPDC) is particularly preferred (col.7, lines 1-10). Porro et al. further teach, "Pyruvate decarboxylase gene promoters...are particularly preferred" (col.7, lines 15-17). Porro et al. describe making a triple deletion of the pyruvate decarboxylase genes encoding PDC1, PDC5, and PDC6, using homologous recombination (col.16, lines 54-67 and col.17, lines 1-20). Porro et al. further teach that "PDC genes are highly conserved among different yeast genera" (col.4, lines 44-45), suggesting that the invention of Porro et al. satisfy all the limitations of claim 16.

Claim 17 is directed to the transformant according to claim 16, wherein the aforementioned host is *Saccharomyces cerevisiae*. Porro et al. teach transformed yeast, *Saccharomyces cerevisiae*.

Claim 18 is directed to a lactic acid manufacturing method provided with a process for culturing the transformant described in claim 1, and a process for separating lactic acid from the cultured product obtained in the aforementioned process. Porro et al. teach, "a process for the preparation of...lactic acid by culturing the above described metabolically engineered yeast strains in a fermentation medium containing a carbon source and recovering lactic acid from the fermentation medium" (col.2, lines 54-58).

Therefore Porro et al. anticipated the instant claims.

Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Weitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SDL/ Scott Long
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